

ABSTRACT

The present invention describes the design, synthesis and therapeutic use of a variety of novel inhibitors of polyamine transport. The main feature of this class of transport inhibitors is to incorporate a linker or side chain that prevents the uptake of polyamines and helps to conjugate polyamine analogs to form dimers with high inhibitory potency against polyamine uptake. These new compounds incorporate features that are designed to maximize their chemical and metabolic stability and their ability to bind to the polyamine transporter, and to minimize their toxicity by preventing their absorption by the cells. The purpose of such inhibitors is to prevent the uptake or salvaging of circulating polyamines by rapidly proliferating cells such as tumor cells, in order to potentiate the effect of therapeutic inhibitors of polyamine biosynthesis such as alpha-difluoromethylornithine.